REMARKS

Claims 68-85 are pending in this application. Claims 78, 79 and 81-85 have been withdrawn by the Examiner as being drawn to non-elected inventions. Claims 68-77 and 80 are under examination.

Applicants have amended claims 68, 70, 72, 80 and 83-85 to clarify the claimed invention. Specifically, Applicant has replaced the term "effective amount" in claims 68 and 83-85 with the term "effective dose." Support for the amendment can be found in the specification as filed at, *inter alia*, page 30, line 33, to page 31, line 9.

Claims 70 and 72, as amended, recite particular bacteria and fungi, respectively, known to cause disease in animals. New claims 86-89 have been added. Support for the amended claims 70 and 72 and new claims 86-89 can be found in the specification as filed, as detailed in the table below:

Claim	Support
70	"a species of *Pseudomonas*" (page 31, lines 20-23) "*Staphylococcus*" (page 11, line 36, to page 12, line 2)
72	"a species of *Aspergillus*" (page 11, lines 29-31)
86	"*Mycobacterium smegmatis*" (Table 9 on page 54) "*Staphylococcus aureus*" (page 18, lines 29-30)
87	"*Aspergillus niger*" (Table 9 on page 54)
88	"has a 16S rRNA gene comprising...as determined by Clustal Analysis" (page 13, lines 29-34)
89	"has a cellular fatty acid composition comprising...about 39% C18:1 (11, 12) fatty acid" (page 13, line 37, to page 14, line 8)

No new matter has been added. Upon entry of the present amendments, claims 68-89 will be pending in the present application.

I. THE WRITTEN DESCRIPTION REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH, SHOULD BE WITHDRAWN

Claims 68-77 and 80 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. The basis for the Examiner's contention is that "[t]he limitation 'an effective amount' of *Burkholderia casidae* or variant in the method for *in vivo* treating or inhibiting diseases or animals or humans lacks support in

the instant specification" (Office Action, page 3, ¶3, lines 1-3). For the following reasons, Applicants respectfully disagree.

1. The Legal Standard

The test for sufficiency of written description is whether the disclosure of the application "reasonably conveys to the artisan that the inventor had possession" of the claimed subject matter. *In re Kaslow*, 707 F.2d 1366, 1375, 217 U.S.P.Q. 1089, 1096 (Fed. Cir. 1983); accord *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563, 19 U.S.P.Q.2d. 1111, 1117 (Fed. Cir. 1991); *see also, Ralston Purina Co. v. Far-Mar-Co, Inc.*, 772 F.2d 1570, 1575, 227 U.S.P.Q. 177, 179 (Fed. Cir. 1985). An applicant can show possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 U.S.P.Q.2d 1961, 1966 (Fed. Cir. 1997). Information which is well known in the art need not be described in detail in the specification. *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d, 1367, 1379-80, 231 U.S.P.Q. 81, 90 (Fed. Cir. 1986).

It is well established that the law does not require the claimed subject matter to be described literally (*i.e.*, using the same words or *in haec verba*) for the disclosure to satisfy the written description requirement. The Court has repeatedly considered the written description requirement and consistently found that exacting detail is not necessary to meet the requirement:

> If a person of ordinary skill in the art would have understood the inventor to have been in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate written description requirement is met.

In re Alton, 76 F.3d 1168, 1175, 37 U.S.P.Q.2d 1578, 1583-84 (Fed. Cir. 1996); *see also In re Lukach*, 442 F.2d 967, 969, 169 U.S.P.Q. 795, 796 (C.C.P.A. 1971) ("the invention claimed does not have to be described in *ipsis verbis* in order to satisfy the description requirement of § 112"). The Court has also held that for purposes of the written description requirement, "examples are not necessary to support the adequacy of a written description." *Falkner v. Inglis*, 448 F.3d 1357, 1366, 79 U.S.P.Q.2d 1001, 1007 (Fed. Cir. 2006).

2. The Specification Provides Sufficient Written Description For The Claims

The Examiner contends that the limitation "an effective amount" has no literal support in the specification by way of a generic disclosure or by way of specific *in vivo* examples (Office Action, page 3, ¶3, lines 3-7). In response, Applicants submit that the relevant case law clearly establishes that the subject matter of the claims need not be described literally in order for the disclosure to satisfy the written description requirement. *In re Alton*, 76 F.3d at 1175. Moreover, examples are also not necessary to support the adequacy of a written description. *Falkner v. Inglis*, 448 F.3d at 1366. The written description requirement is satisfied as long as the specification describes in such a way that a person skilled in the art can reasonably conclude that the inventor(s) had possession of the claimed subject matter. *In re Kaslow*, 707 F.2d at 1375.

Nevertheless, without agreeing with the Examiner and merely to advance prosecution, Applicants have amended claim 68 to recite, in part, administering an "effective dose" of an antimicrobial preparation. Applicants submit that, as used in the instant specification (see, *e.g.*, paragraph bridging pages 30 and 31), the term "effective dose" would be understood by a person skilled in the art to mean an amount of an antimicrobial preparation effective (*i.e.*, "effective amount") to treat or inhibit in an animal a disease caused by a microorganism; thus, the amendment merely clarifies and does not narrow the scope of the claim.

As detailed below, Applicants submit that the disclosure of the application reasonably conveys to a person skilled in the art that the inventors had possession of the invention of amended claim 68 and its dependent claims.

The term "effective dose" is literally described in the specification as filed at, for example, page 30, line 37. Moreover, the specification provides teaching and working examples that demonstrate to the skilled artisan that an effective dose can routinely be determined. For example, the specification describes a disc diffusion test useful for measuring the inhibitory activity of *Burkholderia casidae* strain 2.2N culture, fraction and/or cells on various animal pathogens, such as *Candida albicans*, *Cryptococcus neoformans*, *Aspergillus niger*, *Staphylococcus aureus*, and *Mycobacterium smegmatis*, in which the level of inhibition was assessed by measuring the diameter of the zones of inhibition of the pathogen growth surrounding the spots of *Burkholderia casidae* strain 2.2N culture, fraction

and/or cells (see, *e.g.*, Section 6.2.4 on page 53; Tables 8 and 9 at page 54; Table 10 at page 55; Table 17 at page 65; Tables 19 and 20 at page 66; and Table 21 at page 68).

A person skilled in the art at the time the application was first filed (*i.e.*, April 23, 1997), based on the teaching of the specification coupled with knowledge common in the art at that time, would readily appreciate that the inventors were in possession of an effective dose because standard tests such as the disc diffusion tests described and utilized in the instant specification could be used to routinely calculate an effective dose of an antimicrobial preparation comprising a substantially pure culture or suspension of *Burkholderia casidae* or variant thereof, a cell-free filtrate or cell fraction prepared from a substantially pure culture or suspension of *Burkholderia casidae* or variant thereof, or a cell-free filtrate or cell fraction prepared from an inactivated substantially pure culture or suspension of *Burkholderia casidae* or variant thereof, for treating or inhibiting in an animal a disease caused by a microorganism. As corroboration of this, the Examiner's attention is respectfully directed to the Declaration by Joseph O. Falkinham, III, Ph.D. Under 37 C.F.R. § 1.132 (hereinafter "Falkinham Declaration"), which is being submitted herewith. See, in particular, Falkinham Declaration, ¶¶4-7.

The Examiner next contends that the specification does not describe microorganisms "that are considered as causing diseases of animals not plants," and that "some of the claimed infections are plant pathogens" (Office Action, page 3, ¶3, lines 9-11). Contrary to the Examiner's allegation, the specification describes a number of microorganisms that are known, at the time the application was first filed, to cause diseases in animals (see Falkinham Declaration, ¶6). Also, Applicants submit that it is irrelevant whether certain pathogens that cause diseases in animals can also cause diseases in plants. The fact that some of the pathogens may also be plant pathogens does not obviate the fact that a person skilled in the art would know that those same pathogens are also animal pathogens. Furthermore, claims 70 and 72, as amended, and new claims 86-89 only recite particular pathogens known to cause disease in animals; plant pathogens such as *Alternaria* and *Botrytis* are no longer recited in the claims.

For the foregoing reasons, Applicants submit that the specification, when read as a whole in the context of the state of the art at the time the application was first filed, reasonably conveys to a person skilled in the art that the inventors had possession of the

claimed therapeutic and prophylactic methods. As such, Applicants respectfully requests that the rejection be withdrawn.

II. THE ENABLEMENT REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH SHOULD BE WITHDRAWN

The specification is objected to and claims 68-77 and 80 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the enablement requirement. The basis for the Examiner's contention is that "[t]he 'effective' amounts for in vivo administration and *in vivo* treating or inhibiting microbial infections in animals or humans are not disclosed in the specification by way of generic disclosure or in the working examples" (Office Action, page 6, ¶1, lines 4-6). For the following reasons, Applicants respectfully disagree.

1. The Legal Standard

The enablement requirement refers to the requirement of 35 U.S.C. § 112, first paragraph, that the specification describe (1) how to make and (2) how to use the invention. *See* MPEP § 2164. The test for enablement is whether one reasonably skilled in the art could make or use the invention, without undue experimentation, from the disclosure in the patent specification coupled with information known in the art at the time the patent application was filed. *United States v. Telectronics Inc.*, 857 F.2d 778, 8 U.S.P.Q.2d 1217 (Fed. Cir. 1988). In fact, well known subject matter is preferably omitted. See *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384 (Fed. Cir. 1986) ("a patent need not teach, and preferably omits, what is well known in the art."). Enablement is not precluded even if some experimentation is necessary, provided the experimentation required is merely routine. *In re Wands*, 858 F.2d 731, 737, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988) (citing *In re Jackson*, 217 U.S.P.Q. 804, 807 (Bd. Pat. App. & Inter. 1982)). The fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation. *In re Certain Limited-Charge Cell Culture Microcarriers*, 221 U.S.P.Q. 1165, 1174 (Int'l Trade Comm'n 1983).

By definition, undue experimentation is experimentation that would require a level of ingenuity beyond what is expected from one of ordinary skill in the field. *Fields v. Conover*, 443 F.2d 1386, 1392, 170 U.S.P.Q. 276, 279 (C.C.P.A. 1971). The factors that are relevant

in determining what constitutes undue experimentation as set forth by the Federal Circuit (citing *Ex parte Forman*, 230 U.S.P.Q. 546, 547 (Bd. Pat. App. & Inter. 1986)) include: "(1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims." Any conclusion of nonenablement must be based on the evidence as a whole, and not based on an analysis of only one of the factors while ignoring one or more of the others. *In re Wands*, 858 F.2d at 740.

The Patent Office must establish a *prima facie* case of non-enablement in order to properly reject a claim on that basis. "When rejecting a claim under the enablement requirement of § 112, the Patent Office bears an initial burden of setting forth a reasonable explanation as to why it believes that the scope of protection provided by that claim is not adequately enabled by the description of the invention in the specification of the application..." *In re Wright*, 999 F.2d 1557, 1561, 27 U.S.P.Q.2d 1510, 1513 (Fed. Cir. 1993).

2. <u>The Specification Teaches How To Make And Use The Claimed Invention</u>

The gravamen of the Examiner's rejection appears to be the contention that the specification does not provide "effective" amounts for *in vivo* administration and lacks "*in vivo*" animal data. As discussed above, claim 68 has been amended to recite, in part, administering to said animal an "effective dose" of an antimicrobial preparation. The specification clearly teaches at, for example, page 30, line 33, to page 31, line 9, the concept of "effective dose." The specification also demonstrates that *Burkholderia casidae* strain 2.2N culture, fraction and/or cells are effective at inhibiting the growth of various animal pathogens *in vitro*, wherein the levels of inhibition are measured by the diameter of the respective zone of inhibition (see Section 5.5, at pages 29-31; Section 6.2.4, at page 53; Tables 8 and 9 at page 54; Table 10 at page 55; Table 17 at page 65; Tables 19 and 20 at page 66; and Table 21 at page 68). One skilled in the art could utilize results such as these to routinely calculate an effective dose for *in vivo* administration. In particular, Applicants submit that it would have been clear to a person skilled in the art at the time the application was first filed that, based on the teaching of the specification coupled with knowledge

common in the art at the time the application was first filed, and using only routine experimentation, standard tests such as the disc diffusion test and the dilution test could be used to routinely calculate an effective dose of an antimicrobial preparation comprising a substantially pure culture or suspension of an appropriate *Burkholderia casidae* or variant thereof, a cell-free filtrate or cell fraction prepared from a substantially pure culture or suspension of *Burkholderia casidae* or variant thereof, or a cell-free filtrate or cell fraction prepared from an inactivated substantially pure culture or suspension of *Burkholderia casidae* or variant thereof, for treating or inhibiting in an animal a disease caused by a microorganism (see Falkinham Declaration, ¶¶8-15). Thus, Applicants submit that the specification fully enables the full scope of the claimed subject matter.

In addition, the relevant case law clearly establishes that *in vitro* data is generally sufficient to support therapeutic utility. *See In re Brana*, 51 F.3d 1560, 34 U.S.P.Q. 1436 (Fed. Cir. 1995); *see also*, MPEP § 2107.03, subsection III, at pages 2100-35 and 2100-36. *In vitro* data are often used to assist in the selection and *in vivo* dosing of an antimicrobial agent (see Falkinham Declaration, ¶14). The Examiner has not provided any reasons for a conclusion of lack of correlation for an *in vitro* animal model to the claimed methods.

The Examiner also contends that because the state of the prior art demonstrates that some bacteria belonging to the genus *Burkholderia* are possible opportunistic human pathogens, and because some human pathogens can be isolated from soil, the claimed method "is uncertain and unpredictable in the absence of at least some potential pathogenicity testing" (Office Action, page 6, ¶2). In response, Applicants point out that the claims recite *Burkholderia casidae* or variant thereof (see Section 3.1 at page 6, lines 14-33). The claims do not recite any other *Burkholderia* species, and thus, it is irrelevant as to whether other *Burkholderia* species would be pathogenic to animals. Nevertheless, Applicants submit that a person skilled in the art at the time the application was first filed would have been able to routinely assess the pathogenicity (if any) of a particular *Burkholderia casidae* isolate by testing for virulence genes and genetic traits known in other *Burkholderia* species (see Falkinham Declaration, ¶¶8-11). "[A] patent need not teach, and preferably omits, what is well known in the art." *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d at 1384.

The *Burkholderia casidae* strain 2.2N described in the specification does not display any of the virulence genes known in representative members of the *Burkholderia* genus and is not pathogenic (see Falkinham Declaration, ¶10). Moreover, at the time the application was

first filed, and even today, no pathogenic *Burkholderia casidae* strain has been identified (see Falkinham Declaration, ¶10).

The Examiner further argues that the claimed subject matter is not enabled, by contending that because *Burkholderia casidae* can be isolated from soil, it is not a normal inhabitant of animals or humans. In response, Applicants submit that the mere fact that a microorganism can be isolated from soil does not preclude it from being a member of the normal flora of animals or humans. In fact, at the time the application was first filed, it was known that many microorganisms, including representative members of the *Burkholderia* genus (*e.g.*, *Burkholderia cepacia*, which has also been known as *Pseudomonas cepacia*[1]), could be isolated from soil and are, at the same time, found in the normal flora of human (see Falkinham Declaration, ¶¶16-17).

For the foregoing reasons, Applicants submit that the specification, when read as a whole in the context of the state of the art at the time the application was first filed, enables a person skilled in the art to make and use the claimed invention, without undue experimentation. As such, Applicants respectfully requests that the rejection be withdrawn.

[1] See Nelson *et al.*, "Virulence factors of *Burkholderia cepacia*," FEMS Immunol Med Microbiol. 1994 Feb;8(2):89-97, page 89, col. 1, ¶1, lines 1-3; and Sun *et al.*, "The emergence of a highly transmissible lineage of *cbl*$^+$ of *Pseudomonas* (*Burkholderia*) *cepacia* causing CF centre epidemics in North America and Britain," Nat Med. 1995 July;7(1):661-6, made of record as references C14 and C19, respectively, in the Supplemental Information Disclosure Statement submitted herewith. As set forth in these two references, one skilled in the art would have been aware that the terms "*Pseudomonas cepacia*" and "*Burkholderia cepacia*" refer to the same species of bacteria.

CONCLUSION

Applicants respectfully request entry of the remarks made herein into the file history of the present application. Withdrawal of the Examiner's rejections and an allowance of the application are earnestly requested. If any issues remain in connection herewith, the Examiner is respectfully invited to telephone the undersigned to discuss the same.

Respectfully submitted,

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